

Exhibit H

A Randomized Comparison of Intraoperative PerfecTemp and Forced-Air Warming During Open Abdominal Surgery

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BACKGROUND: The PerfecTemp is an underbody resistive warming system that combines servocontrolled underbody warming with viscoelastic foam pressure relief. Clinical efficacy of the system has yet to be formally evaluated. We therefore tested the hypothesis that intraoperative distal esophageal (core) temperatures with the PerfecTemp (underbody resistive) warming system are noninferior to upper-body forced-air warming in patients undergoing major open abdominal surgery under general anesthesia.

METHODS: Adults scheduled for elective major open abdominal surgery (liver, pancreas, gynecological, and colorectal surgery) under general anesthesia were enrolled at 2 centers. Patients were randomly assigned to underbody resistive or forced-air warming. Resistive heating started when patients were transferred to the operating room table; forced-air warming started after patients were draped. The primary outcome was noninferiority of intraoperative time-weighted average core temperature, adjusted for baseline characteristics and using a buffer of 0.5°C.

RESULTS: Thirty-six patients were randomly assigned to underbody resistive heating and 34 to forced-air warming. Baseline and surgical characteristics were generally similar. We had sufficient evidence ($P = 0.018$) to conclude that underbody resistive warming is not worse than (i.e., noninferior to) upper-body forced-air warming in the time-weighted average intraoperative temperature, with a mean difference of -0.12°C [95% confidence interval (CI) -0.37 to 0.14]. Core temperatures at the end of surgery averaged 36.3°C [95% CI 36 to 36.5] in the resistive warming patients and 36.6°C [95% CI 36.4 to 36.8] in those assigned to forced-air warming for a mean difference of -0.34°C [95% CI -0.69 to 0.01].

CONCLUSIONS: Mean intraoperative time-weighted average core temperatures were no different, and significantly noninferior, with underbody resistive heating in comparison with upper-body forced-air warming. Underbody resistive heating may be an alternative to forced-air warming. (Anesth Analg 2011;113:1076–81)

Perioperative hypothermia is associated with adverse outcomes, including impaired drug metabolism,^{1–3} cardiac morbidity,^{2,4–7} shivering,^{8–10} impaired immune function,^{6,11} coagulopathy,^{11,12} and increased use of hospital resources.^{1,13} As might thus be expected, randomized trials demonstrate that the maintenance of perioperative normothermia significantly reduces morbidity.^{10,12,14,15} Several methods have been developed to help maintain normothermia during surgery, including warming patients before induction of anesthesia,^{16–18} intraoperative use of water mattresses,¹⁹ circulating-water garments,^{20,21} forced-air convection,²² and continuous infusion of warmed liquids.²³

Forced air is by far the most commonly used intraoperative warming approach and has an admirable safety

record.^{19,24} However, a difficulty with forced air is that it is sometimes impossible to warm a sufficient surface area to maintain normothermia during large surgical incision procedures, especially when patients are not supine. Furthermore, the occasional surgeon reports that forced-air warming can be uncomfortable. Finally, some surgeons believe that increasing turbulence in operating rooms increases the risk of wound contamination, although there is overwhelming evidence that it does not.^{25,26}

The PerfecTemp (LMA, San Diego, CA) is an underbody resistive warming system that combines servocontrolled underbody warming with viscoelastic foam pressure relief. An advantage of this resistive heating system is that warming can begin as soon as patients are positioned on the operating room table, whereas forced-air warming is usually delayed until patients are anesthetized and draped for surgery. Because the system does not cover the patient, there is no interference with surgical access; it operates silently; and the system does not use disposables, thus generating no medical waste during routine use. Instead, it replaces the existing operating room table pad and is cleaned between cases just as a standard pad would be (Fig. 1). However, surgical patients lose most heat from the anterior body surface. It is thus unclear whether underbody warming alone, such as provided by the PerfecTemp, will transfer sufficient heat to maintain normothermia during open abdominal surgery.

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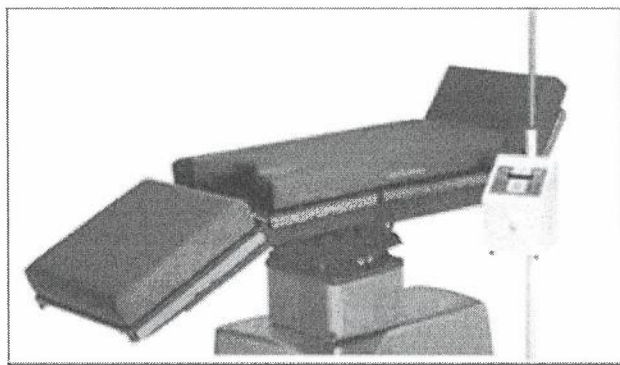


Figure 1. PerfectTemp controller (on pole) and underbody resistive heating pads (on operating room table).

Clinical efficacy of the PerfectTemp system has yet to be formally evaluated. We therefore tested the hypothesis that intraoperative distal esophageal (core) temperatures with the PerfectTemp (underbody resistive) warming system are noninferior to upper-body forced-air warming in patients undergoing major open abdominal surgery under general anesthesia. The secondary hypotheses include that (1) time-weighted average (TWA) intraoperative core temperatures are superior with underbody resistive warming than with upper-body forced-air warming; (2) final intraoperative core temperature is noninferior with underbody resistive warming than with upper-body forced-air warming; and (3) final intraoperative core temperature is superior with underbody resistive warming than with upper-body forced-air warming.

METHODS

We enrolled patients scheduled for elective major open abdominal surgery (liver, pancreas, gynecological, and colorectal surgery) under general anesthesia with an expected operating time of at least 2 hours. Patients were enrolled at the Cleveland Clinic Main Campus in Cleveland, Ohio, and at McMaster University Medical Center in Hamilton, Ontario, Canada. The IRB at each institution approved the study, and written consent was obtained from each participating patient.

Patients were eligible to participate when their body mass index was $<36 \text{ kg/m}^2$, age was 18 to 75 years, ASA physical status was 1 to 3, and the surgical position was supine with or without lithotomy. Patients were excluded when they had a preoperative fever or serious posterior skin lesions.

Protocol

Patients were premedicated with midazolam, fentanyl, or both. Active prewarming was not used. Shortly before transfer to the operating room, patients were randomly assigned to underbody resistive warming or forced-air warming. Randomization (1:1) was based on random blocked computer-generated codes that were maintained in sequentially numbered opaque envelopes; randomization was stratified by site.

In patients who were assigned to underbody resistive warming, the resistive warming system was positioned on the operating room table and set to 40°C about 15 minutes

before the patient entered the operating room. The system was covered by a single-layer sheet and warmed the entire posterior torso of a supine patient. After induction of anesthesia (described below), a single layer of cotton blanket was positioned over the upper body before surgical draping. None of the operating rooms used laminar flow.

The PerfectTemp uses a single primary temperature sensor to servocontrol the heating system (a second system provides safety backup). The control sensor is located at the level of the upper back for a typically sized adult in the conventional supine position. When patients are moved towards the distal end of an operating room table for lithotomy position, the sensor can be at the level of their head. In preliminary studies, we found that use of a foam headrest insulated the sensor from the environment so much that it markedly diminished heat output. In our formal trial, for patients in the lithotomy position, we thus used cotton towels under a foam headrest.

In patients assigned to forced-air warming, an upper-body Bair Hugger (Arizant Medical, Inc., Eden Prairie, MN) cover was positioned over the upper body and exposed arm(s) after induction of anesthesia and covered with a single layer of cotton blanket. The Model 750 forced-air blower was set to "high" (43°C) and activated as soon as practical, usually after prepping and draping. Patients in both groups were otherwise draped per surgical routine. Ambient temperature was maintained near 20°C .

Anesthesia was induced with propofol and fentanyl or sufentanil. Muscle relaxant was given as necessary, and the trachea intubated. Anesthesia was maintained with sevoflurane or desflurane and opioid. Mechanical ventilation was adjusted to maintain end-tidal Pco_2 near 35 mm Hg. Fresh gas flow was generally maintained at a total of 2 L/min. A distal esophageal temperature probe was inserted 40 cm and connected to the anesthesia machine monitoring system. Intravenous and irrigation fluids were warmed to body temperature.

Rescue warming with forced air was initiated if core temperature decreased to $<35^\circ\text{C}$ in patients assigned to underbody resistive warming. The assigned warming system was discontinued if core temperature exceeded 37°C , and restarted if core temperature subsequently decreased to $<37^\circ\text{C}$.

Upon completion of surgery, the esophageal temperature probe was removed and the patient's trachea was extubated after emergence from anesthesia. Subsequent clinical management was at the discretion of the attending anesthesiologist and surgeon. Warmed skin was inspected in the postanesthesia care unit for any thermal changes such as blisters and redness. Skin inspection was repeated on the first postoperative morning.

Measurements

Demographic and morphometric characteristics were recorded. Preoperative sublingual oral temperature was recorded. The number of arms available for forced-air warming was recorded. Whether or not the lithotomy position was used was also recorded.

Time of tracheal intubation was considered elapsed time zero. At 15-minute intervals thereafter, the following variables were recorded: (1) distal esophageal temperature; (2)

Table 1. 2007 Pressure Ulcer Staging System of the National Pressure Ulcer Advisory Panel

Stage	Characteristics
1	Pressure-related changes of intact skin in comparison with the adjacent or opposite areas: <ul style="list-style-type: none"> • Color (nonblanchable redness in lightly pigmented skin; red, blue, or purple hues in darkly pigmented skin). There may also be changes in <ul style="list-style-type: none"> • Temperature (increased warmth or coolness); • Consistency (firm or boggy feel); • Sensation (pain).
2	Partial-thickness skin loss into but not deeper than the dermis, including abrasions, intact or ruptured blisters, and other shallow defects. No exposure of subcutis or deeper structures.
3	Full-thickness skin loss down to subcutaneous fat or, in areas without underlying fat (e.g., nose, malleolus), to fascia, perichondrium, or periosteum. No exposure of muscle, tendon, cartilage, or bone. Sometimes devitalized tissue, undermining, or tunnelling, but that does not hide deeper injury.
4	Full-thickness skin loss with exposure of muscle, tendon, bone, or adjacent structures (e.g., joint spaces). Potentially extensive destruction and increased risk of osteomyelitis.

ambient air temperature at the level of the patient well away from any heat-producing instruments; (3) end-tidal isoflurane, sevoflurane, or desflurane concentration; (4) mean arterial blood pressure; (5) heart rate; and (6) skin temperature at the scapula. Additionally, sublingual oral temperature was recorded 15 minutes after tracheal extubation.

We also recorded the type of volatile anesthetic and the total amounts of fentanyl, sufentanil, propofol, crystalloid, colloid, and blood administered. The following times were recorded: (1) patient transfer to the operating room table; (2) tracheal intubation; (3) forced-air activation; (4) surgical incision; and (5) tracheal extubation. When rescue warming was required, the activation time was recorded.

Subjects' posterior skin integrity was evaluated preoperatively, in the postanesthesia care unit, and on the first postoperative morning using the 2007 Pressure Ulcer Staging system of the National Pressure Ulcer Advisory Panel (Table 1).^{1a} Patients were not told which treatment they received. Investigators and clinicians were not blinded intraoperatively. Postoperative skin integrity evaluations were conducted by an investigator blinded to treatment modality.

Data Analysis

Randomized groups were descriptively compared for balance on baseline potential-confounding variables using the standardized difference, which is the difference in means or proportions divided by the pooled SD. Any baseline variable with a standardized difference of 0.4 or more in absolute value was adjusted for in all of the analyses.

Our primary outcome was intraoperative core temperature. First, we assessed noninferiority of the resistive to forced-air warming in regard to the time-weighted average (TWA) of core temperature from tracheal intubation to 3 hours after or tracheal extubation, whichever came first. Our null hypothesis was that core temperature in the resistive warming group is worse in (lower than) the forced-air group by at least 0.5°C. The noninferiority was assessed using analysis of covariance (ANCOVA), adjusting for the observed imbalance baseline covariables and the preoperative oral temperature. Specifically, we obtained

the parameter estimates for treatment effect (i.e., mean difference between groups) and the corresponding SE from ANCOVA, and then used the results to conduct a 1-tailed 2-sample *t* test with a noninferiority buffer of 0.5°C. The treatment effect was summarized using 95% confidence interval (CI) around the mean difference between groups. The primary analysis was performed according to the intention-to-treat principle.

Randomized groups were also compared on a secondary outcome, the proportion of patients with temperatures above 36°C at the end of surgery, with a logistic regression model, adjusting for preoperative oral temperature and any imbalanced baseline covariables. Furthermore, core temperatures at the end of surgery between randomized groups were compared using 2-sample *t* tests. We assumed that the SD for core temperature would be 0.6°C, as observed in other studies. Sixty patients were needed to show noninferiority of resistive to forced-air warming on the primary outcome with 90% power at the 0.025 significance level. Because some enrolled patients inevitably have shorter operations than anticipated, 70 patients were planned for study inclusion.

SAS software version 9.2 for Windows (SAS Institute, Cary, NC) was used for all statistical analyses, and R software version 2.8.1 for Windows (R Foundation for Statistical Computing, Vienna, Austria) was used for graphics.

RESULTS

Between June and September 2010, 71 patients were enrolled at Cleveland Clinic (*n* = 46) and McMaster University (*n* = 25). One patient was withdrawn because of enrollment in another study. Of 70 patients, 36 patients were randomly assigned to underbody resistive heating and 34 to forced-air warming. In the resistive heating group, 4 patients with core temperatures >35°C were switched to forced-air warming because of clinician preference; 2 others had core temperatures <35°C and were thus switched per protocol to rescue warming with forced air. Meanwhile 2 patients assigned to forced-air warming also reached core temperatures <35°C. Once initiated, rescue warming was continued for the duration of surgery. Fifteen patients reached a core temperature of 37°C during the first 3 operative hours: 6 assigned to resistive heating and 9

^{1a}Available at www.merck.com/mmpe/sec10/ch126/ch126a.html#CACCFBII. Accessed February 12, 2010.

Table 2. Baseline Characteristics and Surgical Factors, by Study Groups

Factor	Resistive (N = 36)	Forced air (N = 34)	Standardized difference*
Age (year)	51 ± 15	51 ± 13	-0.03
Body mass index (kg/m ²)	26 ± 4.2	27 ± 4.3	-0.22
Female	67%	56%	0.22
ASA physical status			0.62
I	6%	3%	
II	44%	74%	
III	50%	24%	
Race (caucasian vs. other)	100%	94%	0.35
Surgical position (supine/lithotomy)	50%	49%	0
Preoperative oral temperature (°C)	36.2 ± 0.9	36.2 ± 0.8	-0.08
Surgical time (hour)	3.7 ± 1.7	3.6 ± 2.2	0.03
Ambient operating room temperature (°C)	20.4 ± 0.7	20.2 ± 0.8	0.26
Number of temperature measurements during first 3 hours	10 ± 2.0	9 ± 2.3	0.31
Arms available during surgery (2 vs. 0)	42%	38%	0.07

Plus-or-minus values are means ± SD. ASA = American Society of Anesthesiologists. Surgical time was from intubation until the last suture. Ambient temperature is presented as time-weighted average.

*Standardized difference (STD) = difference in means or proportions divided by standard error; imbalance defined as absolute value of STD 0.40 (medium effect size).

assigned to forced air. Warming was adjusted as necessary to keep core temperature near 37°C in these patients.

Most baseline characteristics were well balanced between the randomized groups (Table 2). However, patients assigned to resistive heating were more likely to have higher ASA physical status classification. Thus, ASA status was adjusted for in all analyses. Patients in each warming group were given comparable doses of volatile anesthesia and opioid.

We had sufficient evidence ($P = 0.018$) to conclude that underbody resistive warming is not worse than (i.e., non-inferior to) upper-body forced-air warming in the TWA of intraoperative temperature using a noninferiority buffer of 0.5°C. Mean difference (95% CI) of the intraoperative TWA temperature between the groups (resistive heating – forced-air) was -0.12°C (-0.37°C , 0.14°C), adjusting for preoperative oral temperature and ASA physical status (Fig. 2). Noninferiority at the 0.025 significance level is evident because the lower limit of the 95% confidence interval is more than the noninferiority δ of 0.5°C . In a subsequent 1-tailed test, the resistive heating group was not superior to forced-air mean intraoperative TWA temperature ($36.02^{\circ}\text{C} \pm 0.55^{\circ}\text{C}$ vs $36.11^{\circ}\text{C} \pm 0.50^{\circ}\text{C}$, $P = 0.18$), also evident because the confidence interval for the difference between groups overlapped zero. Sensitivity analysis was conducted by including only patients treated per protocol (i.e., a treatment-received analysis); noninferiority was again confirmed.

The proportion of patients above 36°C at the end of surgery in the resistive heating group was smaller than that in the forced-air group (58% vs 88%, multivariable $P = 0.0069$). However, core temperatures at the end of surgery were no different, averaging 36.3 (95% CI, 36 to 36.5) in the resistive warming patients and 36.6 (95% CI, 36.4 to 36.8) in those assigned to forced-air warming, with mean difference (95% CI) of -0.34 (-0.69 , 0.01). There were no adverse events related to the use of either warming system.

DISCUSSION

Forced air is by far the most common perioperative warming approach, presumably because it is effective, safe, and inexpensive. Successful competing warming systems will

Esophageal Temp (°C)

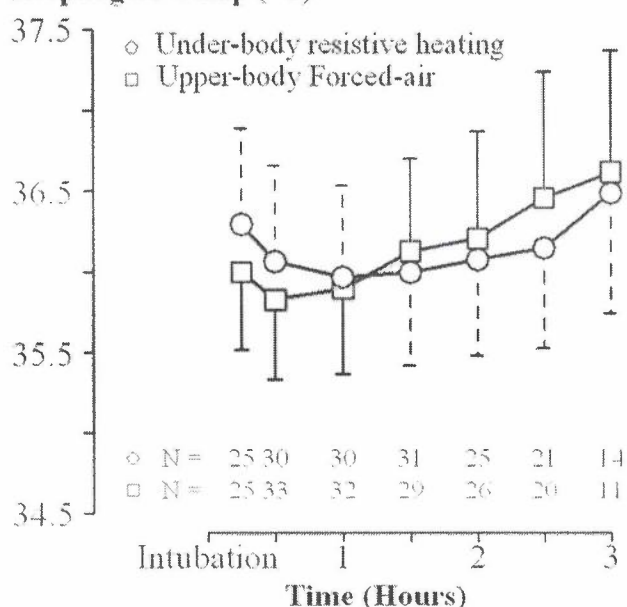


Figure 2. Plot of core temperature over elapsed time during surgery. Temperatures were recorded at 15-minute intervals after elapsed time zero (tracheal intubation). Results are shown as means ± SD.

thus need to match or exceed forced air in these respects, while perhaps providing additional values in terms of convenience, silent operation, or reduced environmental waste. Clinical efficacy of the system we evaluated, the PerfecTemp underbody resistive warming system, was noninferior to forced air. That is, core temperatures were similar with each system, even in the context of open abdominal surgery which provides a strict test of warming efficacy.

Heat can be lost via 4 mechanisms: conduction, evaporation, convection, and radiation. However, little heat, perhaps only 5%, is normally lost to conduction because the foam covering of operating room tables is an excellent thermal insulator; similarly, little heat, perhaps another 10%, is lost to insensible evaporative loss through intact

skin and humidification of dry respiratory gases. A single study in rabbits suggests that considerable heat can be lost to evaporation from within large surgical incisions, although the amount has never been evaluated in humans and for morphologic reasons is surely less than in rabbits. The major routes for intraoperative heat loss are thus convection and radiation, with the later perhaps contributing slightly more. Administration of IV fluids can also cool patients: mean body temperature in a 70-kg patient decreases $\approx 0.25^{\circ}\text{C}$ for each liter of crystalloid given at ambient temperature and by about the same amount for each liter of refrigerated blood.

Convection and radiation both occur at anterior surfaces (including sides of the torso and extremities), and thus anterior surfaces contribute most to intraoperative heat loss. It is thus surprising that posterior warming alone was able to maintain normothermia as well as forced air. Three factors probably contribute to efficacy of the underbody system. The first is that the underbody system was activated even before patients arrive in the operating room. Active patient warming thus started as soon as patients were positioned on the operating room table, whereas forced-air warming was delayed until surgical draping was complete. The second factor is that the surface area available for underbody warming may be larger than with anterior forced-air heating, especially when one or both arms are tucked, as was often the case in our patients. The third factor is that while resistive heating was generated by the posteriorly positioned pad, air warmed by the edges of the pad surely rose and was trapped by the surgical drapes to form a cocoon of warm air over the anterior surface. The combination of these factors appears to have been sufficient as core temperatures were similar with underbody resistive warming and upper-body forced-air warming during open abdominal surgery.

Normal human skin can tolerate most any duration at 43°C so long as the heat is not accompanied by pressure, but even small amounts of pressure markedly reduce tolerance for warming.²⁷ A challenge for any underbody warming system is to provide sufficient heat while assuring that a patient's weight is well distributed without pressure points that could result in pressure-heat necrosis (burns). Conventional circulating-water mattresses distribute pressure poorly and thus occasionally provoke burns.²⁸ The PerfecTemp underbody system attempts to reduce risk, apparently successfully, by using a viscoelastic foam that distributes pressure. We caution, though, that total experience with the PerfecTemp remains limited to a few hundred patients.

The average duration of surgery was 3.6 ± 1.9 hours; the longest operation was 11.7 hours, and 39 surgical cases exceeded 3 hours. Furthermore, scapular skin temperature averaged $35.8^{\circ}\text{C} \pm 1.2^{\circ}\text{C}$, and the highest recorded temperature was only 38.9°C , which in the absence of pressure should be well tolerated. As might be expected, there were no injuries in our trial and Pressure Ulcer Staging scores were zero in all patients, both immediately after anesthesia and the subsequent morning. We caution, though, that clinical experience with underbody resistive warming remains limited and that experience with thousands of patients will be required to confirm that the system can be

used safely over the broad range of patients, including those with fragile skin having long operations.

Our trial was well powered to test our primary and secondary hypotheses; and though we did not identify any safety issues, considerably more experience with the PerfecTemp heating is still needed. Forced-air warmers are now available from many manufacturers and appear to function comparably. It is likely, though, that efficacy and safety of various resistive heating systems differ as a function of the heating element, number and position of temperature sensors, pressure-distributing elements, etc. Results with one underbody resistive heating system should thus be extrapolated to others only with considerable caution.

In summary, mean intraoperative TWA core temperatures were no different, and significantly noninferior, with underbody resistive heating than with upper-body forced-air warming. Underbody resistive heating may be an alternative to forced-air warming. ■■

DISCLOSURES

Name: Cameron Egan.

Contribution: This author helped conduct the study and write the manuscript.

Attestation: Cameron Egan has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.

Conflict of Interest: Cameron Egan reported no conflict of interest.

Name: Ethan Bernstein.

Contribution: This author helped conduct the study and write the manuscript.

Attestation: Ethan Bernstein has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.

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Name: Design Reddy, MD.

Contribution: This author helped conduct the study.

Attestation: Design Reddy has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.

Conflict of Interest: Design Reddy reported no conflict of interest.

Name: Madi Ali, MD.

Contribution: This author helped conduct the study.

Attestation: Madi Ali reviewed the analysis of the data and approved the final manuscript.

Conflict of Interest: Madi Ali reported no conflict of interest.

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Contribution: This author helped conduct the study.

Attestation: James Paul approved the final manuscript.

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Contribution: This author helped analyze the data and write the manuscript.

Attestation: Dongsheng Yang has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.

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Name: Daniel I. Sessler, MD.

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Attestation: Daniel I. Sessler has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.

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REFERENCES

1. Lenhardt R, Marker E, Goll V, Tschernich H, Kurz A, Sessler DI, Narzt E, Lackner F. Mild intraoperative hypothermia prolongs postanesthetic recovery. *Anesthesiology* 1997;87:1318–23
2. Mort TC, Rintel TD, Altman F. The effects of forced-air warming on postbypass central and skin temperatures and shivering activity. *J Clin Anesth* 1996;8:361–70
3. Heier T, Caldwell JE, Sessler DI, Miller RD. Mild intraoperative hypothermia increases duration of action and spontaneous recovery of vecuronium blockade during nitrous oxide–isoflurane anesthesia in humans. *Anesthesiology* 1991;74:815–9
4. Frank SM, Beattie C, Christopherson R, Norris EJ, Perler BA, Williams GM, Gottlieb SO. Unintentional hypothermia is associated with postoperative myocardial ischemia. *Anesthesiology* 1993;78:468–76
5. Frank SM, Fleishy LA, Breslow MJ, Higgins MS, Olson KF, Kelly S, Beattie C. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events: a randomized clinical trial. *JAMA* 1997;277:1127–34
6. Nesh N, Uretzky G, Insler S, Nataf P, Frolkis I, Pineau E, Cantoni E, Bolotin G, Vardi M, Pevni D, Lev-Ran O, Sharony R, Weinbroum AA. Thermo-wrap technology preserves normothermia better than routine thermal care in patients undergoing off-pump coronary artery bypass and is associated with lower immune response and lesser myocardial damage. *J Thorac Cardiovasc Surg* 2005;129:1371–8
7. Nesh N, Wolf T, Kushnir I, David M, Bolotin G, Sharony R, Pizov R, Uretzky G. Novel thermoregulation system for enhancing cardiac function and hemodynamics during coronary artery bypass graft surgery. *Ann Thorac Surg* 2001;72:S1069–76
8. Cheng C, Matsukawa T, Sessler DI, Kurz A, Merrifield B, Lin H, Olofsson P. Increasing mean skin temperature linearly reduces the core-temperature thresholds for vasoconstriction and shivering in humans. *Anesthesiology* 1995;82:1160–8
9. Flacke JW, Flacke WE. Inadvertent hypothermia: frequent, insidious, and often serious. *Semin Anesth* 1983;2:183–96
10. Kurz A, Sessler DI, Narzt E, Bakar A, Lenhardt R, Huemer G. Postoperative hemodynamic and thermoregulatory consequences of intraoperative core hypothermia. *J Clin Anesth* 1995;7:359–66
11. Michelson AD, MacGregor H, Barnard MR, Kestin AS, Rohrer MJ, Valeri RC. Reversible inhibition of human platelet activation by hypothermia in vivo and in vitro. *Thromb Haemostasis* 1994;71:633–40
12. Hofer CK, Worn M, Tavakoli R, Sander L, Maloigne M, Klaghofer R, Zollinger A. Influence of body core temperature on blood loss and transfusion requirements during off-pump coronary artery bypass grafting: a comparison of 3 warming systems. *J Thorac Cardiovasc Surg* 2005;129:838–43
13. Insler SR, O'Connor MS, Leventhal MJ, Nelson DR, Starr NJ. Association between postoperative hypothermia and adverse outcome after coronary artery bypass surgery. *Ann Thorac Surg* 2000;70:175–81
14. Nesh N, Zisman E, Wolf T, Sharony R, Bolotin G, David M, Uretzky G, Pizov R. Strict thermoregulation attenuates myocardial injury during coronary artery bypass graft surgery as reflected by reduced levels of cardiac-specific troponin I. *Anesth Analg* 2003;96:328–35
15. Kurz A, Sessler DI, Lenhardt RA. Study of wound infections and temperature group: perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. *N Engl J Med* 1996;334:1209–15
16. Hynson JM, Sessler DI, Moayeri A, McGuire J, Schroeder M. The effects of pre-induction warming on temperature and blood pressure during propofol/nitrous oxide anesthesia. *Anesthesiology* 1993;79:219–28
17. Just B, Tréviën V, Delva E, Lienhart A. Prevention of intraoperative hypothermia by preoperative skin-surface warming. *Anesthesiology* 1993;79:214–8
18. Camus Y, Celva E, Sessler DI, Lienhart A. Pre-induction skin-surface warming minimizes intraoperative core hypothermia. *J Clin Anesth* 1995;7:384–8
19. Hynson J, Sessler DI. Intraoperative warming therapies: a comparison of three devices. *J Clin Anesth* 1992;4:194–9
20. Taguchi A, Ratnaraj J, Kabon B, Sharma N, Lenhardt R, Sessler DI, Kurz A. Effects of a circulating-water garment and forced-air warming on body heat content and core temperature. *Anesthesiology* 2004;100:1058–64
21. Grocott HP, Mathew JP, Carver EH, Phillips-Bute B, Landolfo KP, Newman MF. A randomized controlled trial of the Arctic Sun Temperature Management System versus conventional methods for preventing hypothermia during off-pump cardiac surgery. *Anesth Analg* 2004;98:298–302
22. Kurz A, Kurz M, Poeschl G, Faryniak B, Redl G, Hackl W. Forced-air warming maintains intraoperative normothermia better than circulating-water mattresses. *Anesth Analg* 1993;77:89–95
23. Smith CE, Desai R, Glorioso V, Cooper A, Pinchak AC, Hagen KF. Preventing hypothermia: convective and intravenous fluid warming versus convective warming alone. *J Clin Anesth* 1998;10:380–5
24. Giesbrecht GG, Ducharme MB, McGuire JP. Comparison of forced-air patient warming systems for perioperative use. *Anesthesiology* 1994;80:671–9
25. Huang JK, Shah EF, Vinodkumar N, Hegarty MA, Greatorex RA. The Bair Hugger patient warming system in prolonged vascular surgery: an infection risk? *Crit Care* 2003;7:R13–6
26. Tumia N, Ashcroft GP. Convection warmers—a possible source of contamination in laminar airflow operating theatres? *J Hosp Infect* 2002;52:171–4
27. Ilaiz PA, Kveen GL, Kokate JY, Leland KJ, Hansen GL, Sparrow EM. Prevention of pressure ulcers by focal cooling: histological assessment in a porcine model. *Wounds: Compendium Clin Res Pract* 1995;7:161–9
28. Gendron FG. Unexplained Patient Burns: Investigating Iatrogenic Injuries. Brea, CA: Quest Publishing Co., Inc., 1988